CCGGGGGAGGCTCTTAGGATGTTGTGCTCCGCGGGGCTCAGACGAAATCTTCTGTGAATGGAAG
AAATGCTTCCAAGCAAACAGCCACTACCAGAACAACTGAGAAAGAGGCCAGAGCGCGAGTTCTC
AAACCCTGATTTCGCAGGAGCCGGAGGGGGATATTGGAGAGAAGGTATTTCCAGTCACGCGCAG
TAACAGACCAGCCAAGGACCAGGACTGGAGTTCTGTTCTACAACGGTGGAACAGTGAACGGTCT
CCAAAGAGATGGAGTACGACGCTTACAACGACTCCGGCATCTATGATGATGAGTACTCTGATGG
CTTTGGCTACTTTGTGGACTTGGAGGAGGCGAGTCCGTGGGAGGCCAAGGTGGCCCCGGTCTTC
CTGGTGGTGATCTACAGCTTGGTGTGCTTCCTCGGTCTCCTAGGCAACGGCCTGGTGATTGTCA
TCGCCACCTTCAAGATGAAGAAGACCGTGAACACTGTGTGGTTTGTCAACCTGGCTGTGGCCGA
CTTCCTGTTCAACATCTTTTTGCCGATGCACATCACCTACGCGGCCATGGACTACCACTGGGTG
TTCGGGAAGGCCATGTGCAAGATCAGCAACTTCTTGCTCAGCCACAACATGTACACCAGCGTCT
TCCTGCTGACTGTCATCAGCTTTGACCGCTGCATCTCCGTGCTGCTCCCCGTCTGGTCCCAGAA
CCACCGCAGCATCCGCCTGGCCTACATGACCTGCTCGGCCGTCTGGGTCCTGGCTTTCTTCTTG
AGCTCCCCGTCCCTTGTCTTCCGGGACACCGCCAACATTCATGGGAAGATAACCTGCTTCAACA
ACTTCAGCTTGGCCGCGCCTGAGTCCTCCCCACATCCCGCCCACTCGCAAGTAGTTTCCACAGG
GTACAGCAGACACGTGGCGGTCACTGTCACCCGCTTCCTTTGCGGCTTCCTGATCCCCGTCTTC
ATCATCACGGCCTGCTACCTTACCATCGTCTTCAAGCTGCAGCGCAACCGCCTGGCCAAGAACA
AGAAGCCCTTCAAGATCATCATCACCATCATCATCACCTTCTTCCTCTGCTGGTGCCCCTACCA
CACCCTCTACCTGCTGGAGCTCCACCACACAGCTGTGCCAAGCTCTGTCTTCAGCCTGGGGCTA
CCCCTGGCCACGGCCGTCGCCATCGCCAACAGCTGCATGAACCCCATTCTGTACGTCTTCATGG
GCCACGACTTCAGAAAATTCAAGGTGGCCCTCTTCTCCCGCCTGGCCAACGCCCTGAGTGAGGA
CACAGGCCCCTCCTCCTACCCCAGTCACAGGAGCTTCACCAAGATGTCGTCTTTGAATGAGAAG
GCTTCGGTGAATGAGAAGGAGACCAGTACCCTCTGAACCTCACCTGGGAATGTCCCCCAAAGGT
GCCACGGCCCAGGGACGCCTAGGGACTTGTCTCCGGAAGTGGGAGACATGCCGGGAGCCTTTGG
GAATGCTCCAACGCCCACTGAATTTTGCACAAGGCGGCTCATGTTTTAAGTGGGGTTCCCAAGT
GTGGACACTCTTCCAGTAAAATGGCAGGCAAGCAACCCGAGCTTCTACAACAGGAGCAGGGGAC
CGACTGTGACTGACTCAGAAAAGGGAGCATTTCTGAAGCCAAGACTTGAGCTGTGACCAACATA
CAGGCCAACATACACGATGTCGCCGTGCATGCCCTGAACATGCTGCGCAGTTTTCGTGGGTGAG
GAAGTTACCGCAAACCCATTGCAGACCTGTTATGGCAACATGACAGTCAAACCAACAAAGCCCA
ATACACCCCAACATCCTCCAAGACCTTGACTTTGGATTTCAGAAGAACGGGGGGTGGGGGGAAC
GAGGACCTGAGGGTTAATTTCGAGCTTGGCGAAGCC (SEQ ID NO:1)

FIGURE 1

underlined = deleted in targeting construct

[ ] = sequence flanking Neo insert in targeting construct

CCGGGGGAGGCTCTTAGGATGTTGTGCTCCGCGGGGCTCAGACGAAATCTTCTGTGAATG
GAAGAAATGCTTCCAAGCAAACAGCCACTACCAGAACAACTGAGAAAGAGGCCAGAGCGC
GAGTTCTCAAACCCTGATTTCGCAGGAGCCGGAGGGGGATATTGGAGAGAAGGTATTTCC
AGTCACGCGCAGTAACAGACCAGCCAAGGACCAGGACTGGAGTTCTGTTCTACAACGGTG
GAACAGTGAACGGTCTCCAAAG[AGATGGAGTACGACGCTTACAACGACTCCGGCATCTA
TGATGATGAGTACTCTGATGGCTTTGGCTACTTTGTGGACTTGGAGGAGGCGAGTCCGTG
GGAGGCCAAGGTGGCCCCGGTCTTCCTGGTGGTGATCTACAGCTTGGTGTGCTTCCTCGG
TC]TCCTAGGCAACGGCCTGGTGATTGTCATCGCCACCTTCAAGATGAAGAAGACCGTGA
ACACTGTGTGGTTTGTCAACCTGGCTGTGGCCGACTTCCTGTTCAACATCTTTTTGCCGA
TGCACATCACCTACGCGGCCATGGACTACCACTGGGTG[TTCGGGAAGGCCATGTGCAAG
ATCAGCAACTTCTTGCTCAGCCACAACATGTACACCAGCGTCTTCCTGCTGACTGTCATC
AGCTTTGACCGCTGCATCTCCGTGCTGCTCCCCGTCTGGTCCCAGAACCACCGCAGCATC
CGCCTGGCCTACATGACCTGCTCGGCCGTCTGGGTCCTGGCTTTCTTCTTGAGCTCCCCG
TCCCTTGTCTTCCGGGACACCGCCAACATTCATGGGAAGATAACCTGCTTCAACAACTTC
AGCTTGGCCGCGCCTGAGTCCTCCCCACATCCCGCCCACTCGCAAGTAGTTTCCACAGGG
TACAGCAGACACGTGGCGGTCACTGTCACCCGCTTCCTTTGCGGCTTCCTGATCCCCGTC
TTCATCATCACGGCCTGCTACCTTACCATCGTCTTCAAGCTGCAGCGCAACCGCCTGGCC
AAGAACAAGAAGCCCTTCAAGATCATCATCACCATCATCATCACCTTCTTCCTCTGCTGG
TGCCCCTACCACACCCTCTACCTGCTGGAGCTCCACCACACAGCTGTGCCAAGCTCTGTC
TTCAGCCTGGGGCTACCCCTGGCCACGGCCGTCGCCATCGCCAACAGCTGCATGAACCCC
ATTCTGTACGTCTTCATGGGCCACGACTTCAGAAAATTCAAGGTGGCCCTCTTCTCCCGC
CTGGCCAACGCCCTGAGTGAGGACACAGGCCC]CTCCTCCTACCCCAGTCACAGGAGCTT
CACCAAGATGTCGTCTTTGAATGAGAAGGCTTCGGTGAATGAGAAGGAGACCAGTACCCT
CTGAACCTCACCTGGGAATGTCCCCCAAAGGTGCCACGGCCCAGGGACGCCTAGGGACTT
GTCTCCGGAAGTGGGAGACATGCCGGGAGCCTTTGGGAATGCTCCAACGCCCACTGAATT
TTGCACAAGGCGGCTCATGTTTTAAGTGGGGTTCCCAAGTGTGGACACTCTTCCAGTAAA
ATGGCAGGCAAGCAACCCGAGCTTCTACAACAGGAGCAGGGGACCGACTGTGACTGACTC
AGAAAAGGGAGCATTTCTGAAGCCAAGACTTGAGCTGTGACCAACATACAGGCCAACATA
CACGATGTCGCCGTGCATGCCCTGAACATGCTGCGCAGTTTTCGTGGGTGAGGAAGTTAC
CGCAAACCCATTGCAGACCTGTTATGGCAACATGACAGTCAAACCAACAAAGCCCAATAC
ACCCCAACATCCTCCAAGACCTTGACTTTGGATTTCAGAAGAACGGGGGGTGGGGGGAAC
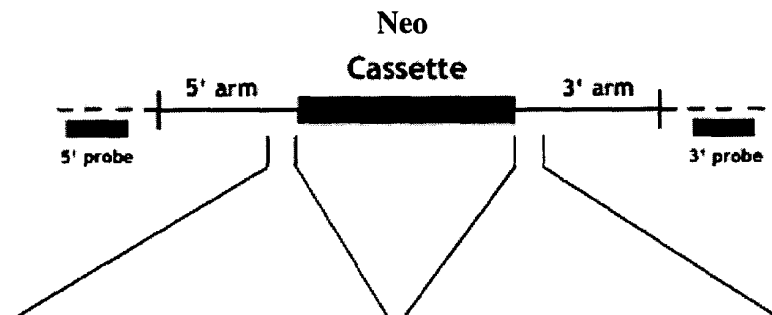GAGGACCTGAGGGTTAATTTCGAGCTTGGCGAAGCC

FIGURE 2A

Gene Sequence Structure *

422 bp   Sequence Deleted   576 bp

Size of full-length
cDNA: 1892 bp

Targeting Vector* (genomic sequence)

Construct Number: 993

Neo
Cassette

5' arm   3' arm

5' probe   3' probe

Arm Length:
5': 2.3 kb
3': 1.9 kb

————— Targeting Vector
– – – – Endogenous Locus
* Not drawn to scale

5'>CCACAGAGGTCCTCAGCCTGT GACCCTGTCTTCCCTCACAGAGAT GGAGTACGACGCTTACAACGACTC CGGCATCTATGATGATGAGTACTC TGATGGCTTTGGCTACTTTGTGGA CTTGGAGGAGGCGAGTCCGTGGGA GGCCAAGGTGGCCCCGGTCTTCCT GGTGGTGATCTACAGCTTGGTGTG CTTCCTCGGTC<3' (SEQ ID NO:2)

5'>TTCGGGAAGGCCATGTGCAAG ATCAGCAACTTCTTGCTCAGCCAC AACATGTACACCAGCGTCTTCCTG CTGACTGTCATCAGCTTTGACCGC TGCATCTCCGTGCTGCTCCCCGTC TGGTCCCAGAACCACCGCAGCATC CGCCTGGCCTACATGACCTGCTCG GCCGTCTGGGTCCTGGCTTTCTTC TTGAGCTCCCC<3' (SEQ ID NO:3)

FIGURE 2B